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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,032	05/10/2006	Sei Kwang Hahn	HAHN5	3877

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

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10/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,032	HAHN ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9,11,20 and 22-30* is/are pending in the application.

4a) Of the above claim(s) *9,11,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8 and 22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 30 Jun 2008, in which claim 1 is amended to change the scope and breadth of the claim; claims 3, 10, 12-19 and 21 are canceled; and new claims 23-30 are added.

This application is the national stage entry of PCT/JP04/16948, filed 15 Nov 2004; and claims benefit of foreign priority documents JAPAN 2003-385054, filed 14 Nov 2003; JAPAN 2003-407681, filed 05 Dec 2003; and JAPAN 2004-259157, filed 07 Sep 2004; currently an English language translation of these foreign priority documents have not been filed.

Claims 1, 2, 4-9, 11, 20 and 22-30 are pending in the current application. Claims 9, 11, 20 and 22, drawn to non-elected species, are withdrawn.

Rejections Withdrawn

Applicant's Amendment, filed 30 Jun 2008, with respect to claims 1, 7, 12 and 18 rejected under 35 USC 112, second paragraph, as being indefinite has been fully considered and is persuasive, as the relative term "dilute" is now defined by amended claim 1 and claims 12 and 18 are canceled. Claim 7 depends from amended claim 1 and incorporates all limitations therein.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Jun 2008, with respect to claims 1, 2, 4-8, 10, 12-18 and 21 rejected under 35 U.S.C. 102(b) as being anticipated by Russell-Jones et al. (US Patent 6,221,397, issued 24 Apr 2001, provided by Applicant in IDS filed 10 May 2006) has been fully considered and is persuasive, as amended claim 1 requires dispersing the solution by spraying to form microparticulate droplets.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Jun 2008, with respect to claims 1, 2, 4-8, 10, 12-18 and 21 rejected under 35 U.S.C. 102(b) as being anticipated by Russell-Jones et al. (US Patent 6,221,397, issued 24 Apr 2001, provided by Applicant in IDS filed 10 May 2006) has been fully considered and is persuasive, as amended claim 1 requires dispersing the solution by spraying to form microparticulate droplets and claims 12-18 and 21 are canceled. Claims 2, 4-8 and 10 depend from amended claim 1 and incorporate all limitations therein

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Jun 2008, with respect to claims 1-8 and 12-19 rejected under 35 U.S.C. 102(b) as being anticipated by Illum et al. (US Patent Application Publication 2001/000765, published 12 Jul 2001, provided by Applicant in IDS filed 10 May 2006) has been fully considered and is persuasive, as amended claim 1 requires the crosslinking reaction is a reaction in which crosslinkages are formed by addition reaction between a mercapto group and an unsaturated C-C bond and claims

12-19 are canceled. Claims 2-8 depend from amended claim 1 and incorporate all limitations therein

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Jun 2008, with respect to claims 1-6 and 12-19 rejected under 35 U.S.C. 102(b) as being anticipated by Yamamoto et al. (US Patent Application Publication 2003/0211166, published 13 Nov 2003, of record) has been fully considered and is persuasive, as amended claim 1 requires the crosslinking reaction is a reaction in which crosslinkages are formed by addition reaction between a mercapto group and an unsaturated C-C bond and claims 12-19 are canceled. Claims 2-6 depend from amended claim 1 and incorporate all limitations therein

This rejection has been **withdrawn**.

Applicant's Amendment, filed 30 Jun 2008, with respect to claims 1, 7, 8, 10, 18, 19, and 21 rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (US Patent Application Publication 2003/0211166, published 13 Nov 2003, of record) in view of Schense et al. (US Patent Application Publication 2003/0012818, 16 Jan 2003, of record) has been fully considered and is persuasive with regard to claims 10, 18, 19 and 21, as claims 10, 18, 19 and 21 are canceled. Applicant remarks that that rejection of claim 1 as anticipated by Yamamoto et al. and the rejection of claim 1 as obvious from Yamamoto et al. are inconsistent. It is noted that the rejection of claim 1 as obvious is over Yamamoto et al. in view of Schense et al., not Yamamoto et al. alone. Claims 7 and 8, rejected as obvious over Yamamoto et al. in view of Schense et

al., depend from claim 1. Claim 1 is rejected as obvious over Yamamoto et al. in view of Schense et al., to make it clear on the record that the limitations of claim 1, which are incorporated into dependent claims 7 and 8, are made obvious over Yamamoto et al. in view of Schense et al. in accordance with treating the subject matter of claim 7 and claim 8 as a whole. Applicant remarks that Yamamoto et al. discloses one embodiment wherein the crosslinking reaction occurs after fabrication of microspheres (Yamamoto et al. example 3 at page 4), however Yamamoto et al. also discloses crosslinking agents co-formulated into the microspheres, the hyaluronic acid starting material partially crosslinked to aid particle formation, and the crosslinking in both non-hydrated and partially hydrated states (Yamamoto et al. page 2, paragraph 30). Therefore the broader disclosure of Yamamoto et al. encompasses the crosslinking reaction occurring during the spray draying procedure disclosed by Yamamoto et al., and the disclosed embodiment does not constitute teaching away from the broader disclosure.

This rejection with regard to claims 10, 18, 19 and 21 has been **withdrawn**. This rejection with regard to claims 1, 7 and 8 is modified as detailed below.

Applicant's Amendment, filed 30 Jun 2008, with respect to claims 12-14, 16-19 and 21 are provisionally rejected on the ground of nonstatutory double patenting over claims 1, 10, 17, 26, 27, 29-32, 35, 36 and 38-41 of copending Application No. 10/536031 has been fully considered and is persuasive, as claims 12-14, 16-19 and 21 are canceled. It is noted that a restriction was not required between claims 12-14, 16-19 and 21, drawn to the product-by-process, and claims drawn to the process of making

said product. Therefore this provisional rejection on the ground of nonstatutory double patenting was proper.

This provisional rejection has been **withdrawn**.

The following new or modified grounds of rejection are necessitated by Applicant's Amendment and Remarks, filed 30 Jun 2008, in which claim 1 is amended to change the scope and breadth of the claim; claims 3, 10, 12-19 and 21 are canceled; and new claims 23-30 are added.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 1, 2, 4-8 and 22-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (US Patent Application Publication 2003/0211166, published 13 Nov 2003, of record) in view of Schense et al. (US Patent Application Publication 2003/0012818, 16 Jan 2003, of record).

Yamamoto et al. discloses microspheres of hyaluronic acid to deliver a drug or active substance (page 2, paragraphs 27 and 28). Yamamoto et al. discloses the microspheres prepared by standard spray drying techniques, in which a solution containing the hyaluronate polymer is dispersed to form atomized, or microparticulate, droplets which condense and dry, concentrating the solution (page 2, paragraph 29). Yamamoto et al. discloses chemical cross-linking of the microspheres co-formulated into the microspheres, added to the starting hyaluronic acid starting material or after fabrication in the partially hydrated state (page 2, paragraph 30). Yamamoto et al. discloses using a starting solution containing 0.5% concentration HA, a dilute solution (page 3, paragraph 37). Yamamoto et al. discloses the process wherein the microspheres have a diameter between 0.01 and 100 microns (page 2, paragraph 28). Yamamoto et al. discloses the process wherein the microspheres are capable of providing a sustained drug delivery effect (page 3, paragraph 36). Yamamoto et al.

discloses drugs or other active agents encapsulated in the microsphere to provide local drug delivery (page 3, paragraph 35).

Yamamoto et al. does not disclose the specific method wherein the specific crosslinking reaction is a reaction in which crosslinkages are formed by addition reaction between a mercapto group and an unsaturated C-C bond (instant claim 1). Yamamoto et al. does not disclose the specific method wherein the dilute solution before the crosslinking reaction contains a drug, and the drug is held in the microparticles obtained after the crosslinking reaction (instant claims 7, 26 and 30). Yamamoto et al. does not disclose the specific method wherein the crosslinking reaction does not cause drug denaturation even in the presence of the drug (instant claims 8 and 27).

Schense et al. teaches bioactive molecules entrapped within a matrix for the controlled delivery of said bioactive molecules wherein said bioactive molecules are exntrapped during gelation of the matrix (page 1, paragraph 12). Schense et al. teaches the matrix formed by the reaction of a multi-thiol, or mercapto groups, and a conjugated unsaturated group in a solution that contains a bioactive molecule, or drug, mixed together to perform the crosslinking reaction (page 6, paragraphs 81 and 82). Schense et al. defines a conjugated unsaturated group to include carbon-carbon bonds (paragraph 25 spanning pages 2 and 3). Schense et al. teaches the matrix-forming reaction is self-selective, meaning the thiol preferentially reacts with the conjugated unsaturated group rather than other biological compounds such as the bioactive molecule, indicating that the matrix-forming reaction does not cause drug denaturation

(page 3, paragraphs 26 and 27). Schense et al. does not explicitly describe the gelation or matrix-forming reaction as a crosslinking reaction, however one of ordinary skill in the art would understand the terms gelation and matrix as described in page 3 paragraphs 29 and 30 to refer to the formation of a crosslinked polymer. Schense et al. teaches the matrix made of natural polymers such as hyaluronic acid (page 3, paragraph 39).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Yamamoto et al. in view of Schense et al. Both Yamamoto et al. and Schense et al. are drawn to crosslinked hyaluronic acid for sustained release of a bioactive molecule. One of ordinary skill in the art at the time of the invention would be motivated to combine the invention of Yamamoto et al. in view of Schense et al. to improve a similar product and process in the same way because Schense et al. teaches the improvement increases the retainable concentration of bioactive molecules in a matrix (Schense et al. page 1, paragraph 9).

Response to Applicant's Remarks:

Applicant's Remarks, filed 30 Jun 2008, have been fully considered and not found to be persuasive.

Applicant remarks that Yamamoto et al. discloses one embodiment wherein the crosslinking reaction occurs after fabrication of microspheres (Yamamoto et al. example 3 at page 4), however Yamamoto et al. also discloses crosslinking agents co-formulated into the microspheres, the hyaluronic acid starting material partially crosslinked to aid particle formation, and the crosslinking in both non-hydrated and partially hydrated states (Yamamoto et al. page 2, paragraph 30). Therefore the broader disclosure of

Yamamoto et al. encompasses the crosslinking reaction occurring in the droplets form in the spray draying procedure disclosed by Yamamoto et al. The disclosed embodiment does not constitute teaching away from the broader disclosure.

The phrase "to facilitate crosslinking reaction of the polysaccharide derivative" is interpreted as the purpose of the active step of "concentrating the solution contained in the droplets". This purpose is inherently present in the active step because it is well known in the art that a chemical reaction rate is a function of the concentrations of reactants, therefore increasing the concentrations of reactants facilitates the reaction by accelerating the rate of reaction. Therefore this statement reciting the purpose of the active step imports no structural or manipulative difference in the recited active step.

Applicant's remarks that Yamamoto et al. in view of Schense et al. does not specifically teach a the reason to combine a crosslinkage reaction with a spray dry procedure. As detailed above, one of ordinary skill in the art at the time of the invention would be motivated to combine the invention of Yamamoto et al. in view of Schense et al. to improve a similar product and process in the same way because Schense et al. teaches the improvement increases the retainable concentration of bioactive molecules in a matrix (Schense et al. page 1, paragraph 9). "The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant." See MPEP 2144 IV.

Amended Claims 1, 2, 4-8 and 22-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Illum et al. (US Patent Application Publication 2001/000765, published 12 Jul 2001, provided by Applicant in IDS filed 10 May 2006) in view of Hubbell et al. (US Patent Application Publication 2002/0177680, published 28 Nov 2002, cited in PTO-892).

Illum et al. discloses a drug incorporated into polysaccharide microspheres prepared by spray drying (page 2, paragraph 22). Illum et al. discloses the polysaccharide solution includes cross-linking agents (page 4, paragraph 43). Illum et al. discloses the spray drying process to atomize the polysaccharide solution into microparticulate droplets, followed by drying, or concentrating the solution in the droplets (page 3, paragraph 35). Illum et al. discloses the use of the polysaccharide hyaluronic acid (page 4, paragraph 39). Illum et al. discloses the method of making said microspheres wherein the resulting particle size is from 0.1 to 10 micrometers (page 4, paragraph 44). Illum et al. discloses the method wherein the microsphere is a sustained-release drug carrier (page 4, paragraphs 40 and 41). Illum et al. discloses the process of preparing a dilute solution, 0.75 g polysaccharide per 20 mL solution, containing the polysaccharide and drug (page 3, paragraph 34), which is 3.75% w/v, prior to the crosslinking reaction, indicating the crosslinking does not cause drug denaturation. Illum et al. discloses the crosslinking agents are chosen from material that will provide total biodegradation of the microparticles (page 4, paragraph 43).

Illum et al. does not disclose the specific method wherein the specific crosslinking reaction is a reaction in which crosslinkages are formed by addition reaction between a mercapto group and an unsaturated C-C bond (instant claim 1).

Hubbell et al. teaches crosslinkers of microgel polyanionic polymers for medical treatments such as drug delivery devices (page 1, paragraphs 1-2). Hubbell et al. defines a microgel to be a particle of 0.1 to 1000 micrometers (page 4, paragraph 46). Hubbell et al. teaches the crosslinkers benefit from hydrolytic sensitivity, namely degradation into smaller components suitable for elimination from the body (page 1, paragraph 5). Hubbell et al. teaches the use of the polyanionic polymer hyaluronic acid (page 1, paragraph 8). Hubbell et al. teaches the preferred embodiment wherein the crosslinker is formed by the reaction of a mercapto group and a vinylic double bond, an unsaturated C-C bond (page 2, paragraph 19).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Illum et al. in view of Hubbell et al. Both Illum et al. and Hubbell et al. are drawn to the art of crosslinked hyaluronic acid polymers for drug delivery. One of ordinary skill in the art would be motivated to combine Illum et al. in view of Hubbell et al. because Illum et al. teaches the crosslinking agents crosslinking agents are chosen from material that will provide total biodegradation of the microparticles and the crosslinkers taught by Hubbell et al. benefit from hydrolytic sensitivity, namely degradation into smaller components suitable for elimination from the body.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jonathan Lau
Patent Examiner
Art Unit 1623

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner
Art Unit 1623